

REMARKS

Claim 18 has been amended to specify that the processor is programmed “to use a first algorithm to obtain a first score from a first test using the fluorescence values and to obtain a second score from a second test using the fluorescence values, and to use the first score and the second score to generate a composite score to determine whether the sample is positive, negative, or indeterminate for the presence of the nucleic acid.” Claim 18 has also been amended to delete improper periods. Support for amended claim 18 is found, for example, on page 13, line 22 through page 14, line 9 and page 14, lines 25-29 of the specification. Claims 19-21 have been amended for consistency with claim 18. New claim 25 combines the subject matter of previous claims 18 and 19.

Applicant wishes to thank Examiner Smith for the courtesies extended by the Examiner in the telephonic interview with Applicant’s undersigned attorney on May 30, 2006. Proposed amendments to claim 18 were discussed. An agreement was not reached with respect to allowance of the claims, but the Examiner indicated that some of the proposed amendments may overcome the rejections. However, the Examiner wishes to review the file history to determine whether the amendments overcome the rejections.

The Examiner has rejected claims 18, 22, and 23 under 35 U.S.C. §§ 102(e) and 102(f) as being anticipated by U.S. Patent No. 6,387,621 by Wittwer et al. (hereinafter the ‘621 patent). Applicant wishes to point out that new claim 25 incorporates the subject matter of previous claim 19 into previous claim 18. Claim 19 was not rejected under §§ 102(e) and 102(f) over the ‘621 patent. Applicant respectfully traverses the Examiner’s rejection as to amended claims 18, 22, and 23. Amended claims 18, 22, and 23 are not anticipated by the ‘621 patent.

Anticipation exists only if all the elements of the claimed invention are present in a product or process disclosed, expressly or inherently, in a single prior art reference.

Hazeltine Corp. v. RCA Corp., 468 U.S. 1228 (1984). Claim 18 has been amended to specify that the processor is programmed “to use a first algorithm to obtain a first score from a first test using the fluorescence values and to obtain a second score from a second test using the fluorescence values, and to use the first score and the second score to generate a composite score to determine whether the sample is positive, negative, or indeterminate for the presence of the nucleic acid.” Thus, amended claims 18, 22, and 23 require that the processor be programmed to use at least two different tests employing two different algorithms, with each test producing a score. The scores are used to generate a composite score for use in determining whether the sample is positive, negative, or indeterminate for the presence of the nucleic acid.

In contrast, the ‘621 patent describes the use of Confidence Band Analysis to establish a baseline fluorescence region for use in making a positive or negative call, but does not describe the multi-test analysis specified in amended claims 18, 22, and 23. In other words, the ‘621 patent does not describe a processor programmed to use two or more different tests employing two or more different algorithms to produce scores that are used to generate a composite score for determining whether the sample is positive, negative, or indeterminate for the presence of the nucleic acid as specified in amended claims 18, 22, and 23. Thus, the ‘621 patent does not anticipate amended claims 18, 22, and 23 because the ‘621 patent does not describe these required elements of amended claims 18, 22, and 23. Withdrawal of the rejection of claims 18, 22, and 23 under 35 U.S.C. §§ 102(e) and 102(f) is respectfully requested.

The Examiner has also rejected claims 19-21 under 35 U.S.C. § 103(b) as being obvious over the ‘621 patent in view of Schork et al. (U.S. Patent No. 6,291,182; hereinafter the ‘182 patent). Applicant respectfully traverses the Examiner’s rejection. The

invention of amended claims 19-21 is not obvious over the '621 patent in view of the '182 patent.

Claim 18 has been amended to specify that the processor is programmed "to use a first algorithm to obtain a first score from a first test using the fluorescence values and to obtain a second score from a second test using the fluorescence values, and to use the first score and the second score to generate a composite score to determine whether the sample is positive, negative, or indeterminate for the presence of the nucleic acid." Thus, dependent claims 19-21 have the same requirements.

The '621 patent describes the use of Confidence Band Analysis to make a positive or negative call to determine whether a nucleic acid is present in a sample. The '621 patent does nothing to suggest a processor programmed to *initiate multiple algorithms during a polymerase chain reaction (PCR) to generate a "composite score to determine whether the sample is positive, negative, or indeterminate for the presence of the nucleic acid*" as required by amended claims 19-21. The '621 patent does nothing to suggest using a composite score to determine whether the sample is positive, negative, or indeterminate for the presence of the nucleic acid. The '621 patent describes Confidence Band Analysis and its use in making positive or negative calls, but does not suggest *composite scores* or making *indeterminate calls* as specified in amended claims 19-21 and as described on page 13, line 22 through page 14, line 9 of the present application.

The '182 patent does nothing to overcome the insufficiencies of the '621 patent in rendering obvious the invention of amended claims 19-21. Accordingly, the combination of the '621 patent and '182 patent does not render obvious the invention of amended claims 19-21. The '182 patent describes a method of correlating a genotype with a detectable phenotypic trait. The method involves 1.) detecting the existence of a genetic marker, and then 2.) analyzing the frequencies with which genetic markers are expressed in

individuals exhibiting a detectable phenotypic trait versus individuals not exhibiting a detectable phenotypic trait. As described in the '182 patent, genetic markers (*e.g.*, polymorphisms) are detected and positioned using PCR-based assays or other methods, such as radiation hybrid (RH) mapping or fluorescence *in situ* hybridization (FISH).

The statistical tests cited by the Examiner in the January 27, 2006 office action and described in the '182 patent (*e.g.*, Expectation-Maximization Method, Wilcoxon rank test, Kolmogorov-Smirnov test, etc.) have nothing to do with the PCR-based assays or any of the other assays for detecting genetic mutations described in the '182 patent. Instead, the statistical tests cited by the Examiner in the '182 patent are used to analyze the frequencies with which genetic markers are expressed in individuals exhibiting a detectable phenotypic trait versus individuals not exhibiting a detectable phenotypic trait *after the genetic mutations are detected* using assays such as PCR, RH mapping, or FISH.

The statistical tests described in the '182 patent are simply used for data analysis of frequencies *after the genetic mutations are detected*. In other words, the PCR reactions described in the '182 patent must be complete and the data from the PCR reactions must be analyzed (*i.e.*, to determine whether a genetic mutation exists) before an algorithm is even used to determine the frequency with which a genetic marker is associated with a detectable phenotypic trait. Thus, the '182 patent provides no suggestion of initiating analysis algorithms prior to completion of temperature cycling or even applying analysis algorithms directly to PCR. Moreover, the '182 patent does nothing to suggest obtaining composite scores by initiating analysis algorithms prior to completion of temperature cycling or making indeterminate calls based on analysis algorithms initiated prior to completion of temperature cycling.

Accordingly, the '182 patent cannot suggest *initiating multiple algorithms prior to completion of temperature cycling in a PCR reaction to generate “a composite*

score to determine whether the sample is positive, negative, or indeterminate for the presence of the nucleic acid" as required by amended claims 19-21. Thus, neither the '621 patent nor the '182 patent suggests *initiating multiple algorithms prior to completion of temperature cycling in a PCR reaction to generate "a composite score to determine whether the sample is positive, negative, or indeterminate for the presence of the nucleic acid*" as required by amended claims 19-21, and the combination of the '621 patent and the '182 patent is insufficient in making this suggestion. Therefore, the combination of the '621 patent and the '182 patent does not render obvious the invention of claims 19-21.

Withdrawal of the rejection of claims 19-21 under 35 U.S.C. § 103(b) over the '621 patent in view of the '182 patent is respectfully requested.

Further, regarding new claim 25, which requires that "the plurality of tests comprises a Confidence Interval Test and a Signal-to-Noise Ratio Test," the Examiner has conceded (page 5, paragraph 4 of the January 27 office action) that "Wittwer does not teach all of the plurality of tests as stated in instant claims 19-21" from which scores are obtained using fluorescence values. Thus, the Examiner has conceded that the '621 patent does not teach a plurality of tests comprising the Confidence Interval Test and the Signal-to-Noise Ratio Test, from which scores are obtained using fluorescence values, as required by new claim 25.

The '182 patent does not overcome this insufficiency of the '621 patent. Although the Examiner cites to the '182 patent, column 47, lines 29-43, for disclosure of a Signal-to-Noise Ratio Test, the '182 patent teaches in column 47, lines 29-43 that a particular signal may be due to a polymorphism or to noise. To exclude such an artifact, both DNA strands are sequenced. A polymorphism is identified only if detected on both strands. There is nothing in column 47, lines 29-43, to indicate that the analysis outputs a value or a score. The analysis described is simply a confirmation based on detection of a polymorphism on

both DNA strands. Thus, the '182 patent does not overcome the insufficiency of the '621 patent, noted by the Examiner. The '182 patent does not teach a plurality of tests comprising *the Signal-to-Noise Ratio Test, from which scores are obtained* using fluorescence values, as required by new claim 25. Accordingly, new claim 25 is not obvious over the '621 patent in combination with the '182 patent.

CONCLUSION

The foregoing amendments and remarks are believed to fully respond to the Examiner's rejections. The amended claims are in condition for allowance. Applicant respectfully requests allowance of the claims, and passage of the application to issuance.

Respectfully submitted,


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